short-time reduction of systolic function just before childbirth and a significant alteration of the left ventricular diastolic filling pattern (abnormal relaxation pattern). While the left ventricular systolic function was normalized in all patients one week after childbirth left ventricular hypertrophy and left ventricular diastolic dysfunction persisted for nearly two months.

1168-27 Heterogeneity of the Regional Isovolumic Relaxation Time of the Left Ventricular by Pulsed Doppler Tissue Imaging

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Pulsed Doppler tissue imaging (DTI) is a recently developed non invasive technique that has the advantage to analyze the time velocity sequential changes of the diastolic relaxation process. The purpose of this study was to establish the pattern of segmental distribution of the regional isovolumic relaxation time (RIVRT/msec) of the left ventricular (LV) myocardium under normal physiologic conditions. After a transthoracic two-dimensional, color and pulsed DTI studies, we divided the left ventricle (LV) of 40 healthy volunteers, mean age 59 ± 18 years, in 16 different wall segments according to the ASE guidelines of regional wall motion. The pulsed DTI sample was positioned in the middle of the LV wall thickness of each segment. To calculate RIVRT, we measured the time interval from the second heart sound of the phonocardiogram recording to the onset at baseline of early myocardial wall motion of the pulsed DTI profile of each LV myocardial wall segment.

Results: The mean values of the RIVRT ranged from 35.3 ± 18 msec to 76.3 ± 25 msec, with a mean LV value of 52.9 ± 21.5 msec. The mean percentage of variation between the LV myocardial wall segments was 17 ± 16%, range −33% to 44%. When each level of LV wall segment was considered, the mean RIVRT at the basal segments was 48.9 ± 17.6 msec (−7.5%), at the medial segments 54.8 ± 22.4 msec ($p = 0.02$; 3.5%) and at the distal segments 56.3 ± 26 msec ($p = 0.01$; 6.4%). When all segments of each LV wall were studied, the mean RIVRT of the anterior wall was 48.5 ± 22.3 msec (−8.3%; $p = 0.02$), IVS was 57.9 ± 21 msec (9.4%; $p = 0.02$), lateral wall 46 ± 21.2 msec (−13%; $p = 0.01$), postero-inferior wall was 52.5 ± 21.4 msec (−2%; p = ns).

Conclusion: An heterogeneous pattern of the left ventricular regional isovolumic relaxation time was detected in the segmental levels and myocardial walls using pulsed Doppler tissue imaging. The isovolumic relaxation time was shorter at the basal segments compared to the distal regions. This fact reflects the presence of preferential pathways of repolarization and relaxation within the myocardial wall, and could be useful in the detailed evaluation of the myocardial pathophysiology.

1168-28 Effects of the Intracoronary Infusion of Cocaine on Left Ventricular Systolic and Diastolic Function in Humans

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Background: In dogs, a large amount of cocaine causes a marked deterioration of left ventricular (LV) systolic function and an increase in LV end-diastolic pressure. This study was done to assess the influence of a high intracoronary cocaine concentration on LV systolic and diastolic function in humans.

Methods: In 20 patients (14 men and 6 women, aged 39 to 72 years) referred for cardiac catheterization, heart rate, arterial pressure, LV pressure and dP/dt, and LV volumes and ejection fraction were measured before and during the final 2–3 minutes of a 15 minute intracoronary infusion of saline (n = 10, controls) or cocaine hydrochloride, 1 mg/min (n = 10).

Results: No variable changed with saline. With cocaine, the drug concentration in blood obtained from the coronary sinus was 3.0 ± 0.4 (mean ± SD) mg/L, similar in magnitude to the blood cocaine concentration reported in abusers dying of cocaine intoxication. Cocaine induced no significant change in heart rate, LV dP/dt, or LV end-diastolic volume, but it caused an increase in systolic and mean arterial pressure, LV end-diastolic pressure (15 ± 7 to 22 ± 9 mmHg, $p = 0.001$), and LV end-systolic volume, as well as a decrease in LV ejection fraction (0.55 ± 0.13 to 0.50 ± 0.14, $p = 0.03$).

Conclusions: In humans, the intracoronary infusion of cocaine, sufficient in amount to achieve a high coronary sinus concentration, causes a deterioration of LV systolic and diastolic performance.

1169 Valvular Heart Disease

Wednesday, April 1, 1998, 9:00 a.m.–11:00 a.m.
Georgia World Congress Center, West Exhibit Hall Level
Presentation Hour: 9:00 a.m.–10:00 a.m.

1169-18 Aortic Regurgitation Alters the Expression of Dihydropyridine-sensitive L-type Calcium Channels in Cardiac Fibroblasts

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Background: Experimentally, cardiac fibrosis contributes to heart failure (CHF) development (d) in aortic regurgitation (AR). Recent clinical data suggest that CHFd in AR is retarded by treatment with dihydropyridines (DHP), which specifically bind to L-type calcium channels. The basis of this clinical effect is unclear. To determine if DHP effects may relate to cardiac fibrosis in AR, we assessed expression of the DHP-receptor-α_2 chain gene in cardiac fibroblasts (CF).

Methods: Total RNA, extracted from CF primary cultures developed from 2 NZW rabbits with surgically-induced AR and 2 NZW nls, underwent agarose gel electrophoresis, northern-blotting to a nylon filter and probing with a ^{32}P-labeled full-length α_2 chain cDNA fragment. Rabbit skeletal muscle RNA (with the α_2 chain) was probed for comparison; the "housekeeping gene", GAPDH, also was probed to "normalize" results for quantification. RT-PCR of total CF RNA (AR and nl) then was performed with primers specific for α_2-chain.

Results: The α_2 chain band was apparent in 2/2 normal CF lines. Northern blot analysis of mRNA from AR CF, normalized for GAPDH, revealed marked up-regulation of this message in 2/2 AR CF lines. RT-PCR identified α_2-chain mRNA in AR and nl CF.

Conclusion: The DHP-receptor is expressed in nl CF; thus, DHP may affect CF function. DHP-receptor gene expression is up-regulated in AR, a potential basis for enhanced DHP effect on CF. Further studies now must assess the effect of DHP therapy on cardiac fibrosis in AR.

1169-19 Natriuretic Peptides in Patients With Mitral Regurgitation: Markers of Degree or Consequences of the Regurgitation?

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Mitral regurgitation (MR) is associated with left atrial (LA) and ventricular (LV) overload which are known triggers for Natriuretic peptides activation. However, the degree of activation of atrial (ANP) and brain (BNP) natriuretic peptides and cyclic guanosine monophosphate (cGMP) in MR and their potential role as markers of the degree of MR is unknown. In a prospective study of 79 patients with organic MR (age 64 ± 14 years), the regurgitant fraction (RF, mean = 45 ± 17%), LA volume, LV end-systolic volume (ESVI), Systolic pulmonary artery pressure (S-PAP) were measured by Doppler echocardiography simultaneously to ANP, BNP and cGMP measurement by Radioimmunoassay. As compared to age and sex matched controls, ANP (1486 ± 1333 vs 865 ± 624 pg/mL, $P = 0.003$), BNP (67 ± 88 vs 22 ± 36 pg/mL, $P < 0.001$) and cGMP (5 ± 3.6 vs 3.2 ± 2.7 pmoles/mL, $P = 0.037$) were elevated in MR. In patients with MR the RF showed weak correlations to the hormonal levels of BNP ($r = 0.23$, $P = 0.046$) and no significant correlation to ANP and cGMP ($P = 0.4$ and 0.1). Conversely, significant correlations were observed between hormonal levels and hemodynamic alterations:

	ANP	BNP	cGMP
LA volume (mL)	r = 0.38	r = 0.54	r = 0.45
LV ESVI (mL/m2)	NS	r = 0.35	NS
S-PAP (mmHg)	r = 0.22	r = 0.42	r = 0.27
CHF class	r = 0.46	r = 0.66	r = 0.41

In multivariate analysis, the independent determinant of hormonal levels were CHF class ($P = 0.0001$) and age ($P = 0.03$) for ANP, CHF class ($P = 0.0001$), age ($P = 0.0002$) and ESVI ($P = 0.01$) for BNP and LA volume ($P = 0.0001$) and cardiac index ($P = 0.03$) for cGMP. *We Conclude* that in patients with MR, Na iurstic peptides 1) are significantly activated, 2) show no or poor association to the degree of MR for which they cannot serve as markers but 3) are associated to hemodynamic alterations and LV and LA remodeling suggesting that their clinical role in MR should be further investigated.